

SEQUENCE LISTING

<110> DOI, TOSHIO
ABE, HIDEHARU

<120> METHOD AND KIT FOR DETECTING PROLIFERATIVE DISEASES
CAUSING SCLEROSIS, PROPHYLACTIC AND/OR THERAPEUTIC
AGENT FOR PROLIFERATIVE DISEASES CAUSING SCLEROSIS, AND
METHOD AND KIT FOR IDENTIFYING SUBSTANCES EFFECTIVE IN
PREVENTING AND/OR TREATING PROLIFERATIVE DISEASES
CAUSING SCELEROSIS

<130> 10084-0004-00000

<140> 10/571,511

<141> 2006-03-10

<150> PCT/JP04/13124

<151> 2004-09-09

<150> JP 2003-319538

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<170> PatentIn Ver. 3.3

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Arg Ile Asn Ile Tyr Glu Val Met Lys Pro Pro Ala Glu Val Val Pro	
180 185 190	
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Gly His Leu Ile Thr Arg Leu Leu Asp Thr Arg Leu Val His His Asn	
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Val Thr Arg Trp Glu Thr Phe Asp Val Ser Pro Ala Val Leu Arg Trp	
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Thr Arg Glu Lys Gln Pro Asn Tyr Gly Leu Ala Ile Glu Val Thr His	
225 230 235 240	
ctc cat cag act cgg acc cac cag ggc cag cat gtc agg att agc cga	1245
Leu His Gln Thr Arg Thr His Gln Gly Gln His Val Arg Ile Ser Arg	
245 250 255	
tcg tta cct caa ggg agt ggg aat tgg gcc cag ctc cgg ccc ctc ctg	1293
Ser Leu Pro Gln Gly Ser Gly Asn Trp Ala Gln Leu Arg Pro Leu Leu	
260 265 270	
gtc acc ttt ggc cat gat ggc cgg ggc cat gcc ttg acc cga cgc cgg	1341
Val Thr Phe Gly His Asp Gly Arg Gly His Ala Leu Thr Arg Arg Arg	
275 280 285	
agg gcc aag cgt agc cct aag cat cac tca cag cgg gcc agg aag aag	1389
Arg Ala Lys Arg Ser Pro Lys His His Ser Gln Arg Ala Arg Lys Lys	
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Asn Lys Asn Cys Arg Arg His Ser Leu Tyr Val Asp Phe Ser Asp Val	
305 310 315 320	
ggc tgg aat gac tgg att gtg gcc cca cca ggc tac cag gcc ttc tac	1485
Gly Trp Asn Asp Trp Ile Val Ala Pro Pro Gly Tyr Gln Ala Phe Tyr	
325 330 335	
tgc cat ggg gac tgc ccc ttt cca ctg gct gac cac ctc aac tca acc	1533
Cys His Gly Asp Cys Pro Phe Pro Leu Ala Asp His Leu Asn Ser Thr	
340 345 350	

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 Asn His Ala Ile Val Gln Thr Leu Val Asn Ser Val Asn Ser Ser Ile
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ccc aaa gcc tgt tgt gtg ccc act gaa ctg agt gcc atc tcc atg ctg 1629
 Pro Lys Ala Cys Cys Val Pro Thr Glu Leu Ser Ala Ile Ser Met Leu
 370 375 380

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 Tyr Leu Asp Glu Tyr Asp Lys Val Val Leu Lys Asn Tyr Gln Glu Met
 385 390 395 400

gta gta gag gga tgt ggg tgc cgc tga gatcaggcag tccttgagga 1724
 Val Val Glu Gly Cys Gly Cys Arg
 405

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<220>
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<220>
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Gln Leu His Gln Leu Tyr Ser Asp Ser Phe Pro Met Glu Leu Arg Gln	
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Phe Leu Ala Pro Trp Ile Glu Ser Gln Asp Trp Ala Tyr Ala Ala Ser	
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Lys Glu Ser His Ala Thr Leu Val Phe His Asn Leu Leu Gly Glu Ile	
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cac aat cta cga aga atc aag cag ttt ctt cag agc agg tat ctt gag	528
His Asn Leu Arg Arg Ile Lys Gln Phe Leu Gln Ser Arg Tyr Leu Glu	
85 90 95	
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Lys Pro Met Glu Ile Ala Arg Ile Val Ala Arg Cys Leu Trp Glu Glu	
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Ser Arg Leu Leu Gln Thr Ala Ala Thr Ala Ala Gln Gln Gly Gly Gln	
115 120 125	
gcc aac cac ccc aca gca gcc gtg gtg acg gag aag cag cag atg ctg	672
Ala Asn His Pro Thr Ala Ala Val Val Thr Glu Lys Gln Gln Met Leu	
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Glu Gln His Leu Gln Asp Val Arg Lys Arg Val Gln Asp Leu Glu Gln	
145 150 155 160	
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Lys Met Lys Val Val Glu Asn Leu Gln Asp Asp Phe Asp Phe Asn Tyr	
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Lys Thr Leu Lys Ser Gln Gly Asp Met Gln Asp Leu Asn Gly Asn Asn	
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Gln Ser Val Thr Arg Gln Lys Met Gln Gln Leu Glu Gln Met Leu Thr	
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Ala Leu Asp Gln Met Arg Arg Ser Ile Val Ser Glu Leu Ala Gly Leu	
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Leu Ser Ala Met Glu Tyr Val Gln Lys Thr Leu Thr Asp Glu Glu Leu	
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Ala Asp Trp Lys Arg Arg Gln Gln Ile Ala Cys Ile Gly Gly Pro Pro	
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Ser Gln Leu Gln Thr Arg Gln Gln Ile Lys Lys Leu Glu Glu Leu Gln	
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Gln Lys Val Ser Tyr Lys Gly Asp Pro Ile Val Gln His Arg Pro Met	
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Phe Val Val Glu Arg Gln Pro Cys Met Pro Met His Pro Asp Arg Pro	
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Val Lys Phe Pro Glu Leu Asn Tyr Gln Leu Lys Ile Lys Val Cys Ile	
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Asp Lys Asp Ser Gly Asp Val Ala Ala Leu Arg Gly Ser Arg Lys Phe	
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Asn Ile Leu Gly Thr Asn Thr Lys Val Met Asn Met Glu Glu Ser Asn	
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Asn Gly Ser Leu Ser Ala Glu Phe Lys His Leu Thr Leu Arg Glu Gln	
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Thr Glu Glu Leu His Leu Ile Thr Phe Glu Thr Glu Val Tyr His Gln	
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Gly Leu Lys Ile Asp Leu Glu Thr His Ser Leu Pro Val Val Val Ile	
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Ser Asn Ile Cys Gln Met Pro Asn Ala Trp Ala Ser Ile Leu Trp Tyr	
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Pro Ile Gly Thr Trp Asp Gln Val Ala Glu Val Leu Ser Trp Gln Phe	
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Ser Ser Thr Thr Lys Arg Gly Leu Ser Ile Glu Gln Leu Thr Thr Leu	
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gca gag aaa ctc ttg gga cct ggt gtg aat tat tca ggg tgt cag atc	1872
Ala Glu Lys Leu Leu Gly Pro Gly Val Asn Tyr Ser Gly Cys Gln Ile	
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ctg gcc ctt tgg aac gaa ggg tac atc atg ggc ttt atc agt aag gag	2016
Leu Ala Leu Trp Asn Glu Gly Tyr Ile Met Gly Phe Ile Ser Lys Glu	
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Glu Lys Asp Ile Ser Gly Lys Thr Gln Ile Gln Ser Val Glu Pro Tyr	
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Tyr Lys Ile Met Asp Ala Thr Asn Ile Leu Val Ser Pro Leu Val Tyr	
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acc att gac ctg ccg atg tcc ccc cgc act tta gat tca ttg atg cag 2448
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ccc atg tga ggagctgaga acggaagctg cagaaagata cgactgaggc 2593
 Pro Met
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aca tta gct tca ggg tgt atg aaa tat gaa gga tct gat ttt cag tgc 878
Thr Leu Ala Ser Gly Cys Met Lys Tyr Glu Gly Ser Asp Phe Gln Cys
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aaa gat tct cca aaa gcc cag cta cgc cgg aca ata gaa tgt tgt cgg 926
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acc aat tta tgt aac cag tat ttg caa ccc aca ctg ccc cct gtt gtc 974
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195 200 205	
aaa gac ctt att gac cag tca caa agt tct ggt agt ggg tct gga cta	1214
Lys Asp Leu Ile Asp Gln Ser Gln Ser Ser Gly Ser Gly Ser Gly Leu	
210 215 220	
cct tta ttg gtt cag cga act att gcc aaa cag att cag atg gtc cgg	1262
Pro Leu Leu Val Gln Arg Thr Ile Ala Lys Gln Ile Gln Met Val Arg	
225 230 235	
caa gtt ggt aaa ggc cga tat gga gaa gta tgg atg ggc aaa tgg cgt	1310
Gln Val Gly Lys Gly Arg Tyr Gly Glu Val Trp Met Gly Lys Trp Arg	
240 245 250	
ggc gaa aaa gtg gcg gtg aaa gta ttc ttt acc act gaa gaa gcc agc	1358
Gly Glu Lys Val Ala Val Lys Val Phe Phe Thr Thr Glu Glu Ala Ser	
255 260 265 270	
tgg ttt cga gaa aca gaa atc tac caa act gtg cta atg cgc cat gaa	1406
Trp Phe Arg Glu Thr Glu Ile Tyr Gln Thr Val Leu Met Arg His Glu	
275 280 285	
aac ata ctt ggt ttc ata gcg gca gac att aaa ggt aca ggt tcc tgg	1454
Asn Ile Leu Gly Phe Ile Ala Ala Asp Ile Lys Gly Thr Gly Ser Trp	
290 295 300	
act cag ctc tat ttg att act gat tac cat gaa aat gga tct ctc tat	1502
Thr Gln Leu Tyr Leu Ile Thr Asp Tyr His Glu Asn Gly Ser Leu Tyr	
305 310 315	
gac ttc ctg aaa tgt gct aca ctg gac acc aga gcc ctg ctt aaa ttg	1550
Asp Phe Leu Lys Cys Ala Thr Leu Asp Thr Arg Ala Leu Leu Lys Leu	
320 325 330	
gct tat tca gct gcc tgt ggt ctg tgc cac ctg cac aca gaa att tat	1598
Ala Tyr Ser Ala Ala Cys Gly Leu Cys His Leu His Thr Glu Ile Tyr	
335 340 345 350	
ggc acc caa gga aag ccc gca att gct cat cga gac cta aag agc aaa	1646
Gly Thr Gln Gly Lys Pro Ala Ile Ala His Arg Asp Leu Lys Ser Lys	
355 360 365	

aac atc ctc atc aag aaa aat ggg agt tgc tgc att gct gac ctg ggc	1694
Asn Ile Leu Ile Lys Lys Asn Gly Ser Cys Cys Ile Ala Asp Leu Gly	
370 375 380	
ctt gct gtt aaa ttc aac agt gac aca aat gaa gtt gat gtg ccc ttg	1742
Leu Ala Val Lys Phe Asn Ser Asp Thr Asn Glu Val Asp Val Pro Leu	
385 390 395	
aat acc agg gtg ggc acc aaa cgc tac atg gct ccc gaa gtg ctg gac	1790
Asn Thr Arg Val Gly Thr Lys Arg Tyr Met Ala Pro Glu Val Leu Asp	
400 405 410	
gaa agc ctg aac aaa aac cac ttc cag ccc tac atc atg gct gac atc	1838
Glu Ser Leu Asn Lys Asn His Phe Gln Pro Tyr Ile Met Ala Asp Ile	
415 420 425 430	
tac agc ttc ggc cta atc att tgg gag atg gct cgt cgt tgt atc aca	1886
Tyr Ser Phe Gly Leu Ile Ile Trp Glu Met Ala Arg Arg Cys Ile Thr	
435 440 445	
gga ggg atc gtg gaa gaa tac caa ttg cca tat tac aac atg gta ccg	1934
Gly Gly Ile Val Glu Glu Tyr Gln Leu Pro Tyr Tyr Asn Met Val Pro	
450 455 460	
agt gat ccg tca tac gaa gat atg cgt gag gtt gtg tgt gtc aaa cgt	1982
Ser Asp Pro Ser Tyr Glu Asp Met Arg Glu Val Val Cys Val Lys Arg	
465 470 475	
ttg cgg cca att gtg tct aat cgg tgg aac agt gat gaa tgt cta cga	2030
Leu Arg Pro Ile Val Ser Asn Arg Trp Asn Ser Asp Glu Cys Leu Arg	
480 485 490	
gca gtt ttg aag cta atg tca gaa tgc tgg gcc cac aat cca gcc tcc	2078
Ala Val Leu Lys Leu Met Ser Glu Cys Trp Ala His Asn Pro Ala Ser	
495 500 505 510	
aga ctc aca gca ttg aga att aag aag acg ctt gcc aag atg gtt gaa	2126
Arg Leu Thr Ala Leu Arg Ile Lys Lys Thr Leu Ala Lys Met Val Glu	
515 520 525	
tcc caa gat gta aaa atc tga tgggttaaacc atcggaggag aaactctaga	2177
Ser Gln Asp Val Lys Ile	
530	
ctgcaagaac tgtttttacc catggcatgg gtggaattag agtgggaataa ggatgttaac	2237
ttgggttctca gactctttct tcaactacgtg ttcacaggct gctaataatta aacctttcag	2297
tactcttatt aggatacaag ctgggaactt ctaaactt cattctttat atatggacag	2357
ctttatttta aatgtgggtt ttgatgcctt tttttaagtg ggtttttatg aactgcatca	2417
agacttcaat cctgattagt gtctccagtc aagctctggg tactgaattg cctgttcata	2477
aaacggtgct ttctgtgaaa gccttaagaa gataaatgag cgcagcagag atggagaaat	2537
agactttgcc ttttacctga gacattcagt tcgtttgtat tctacctttg taaaacagcc	2597

tatagatgat gatgtgtttg ggatactgct ttttttatga tagtttgtcc tgtgtcctta 2657
 gtgatgtgtg tgtgtctcca tgcacatgca cgccgggatt cctctgctgc catttgaatt 2717
 agaagaaaat aatttatatg catgcacagg aagatattgg tggccggtgg ttttgtgctt 2777
 taaaaatgca atatctgacc aagattcgcc aatctcatac aagccattta ctttgcaagt 2837
 gagatagctt ccccaccagc tttatTTTTT aacatgaaag ctgatgcaa ggccaaaaga 2897
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 cttaaaaga aagcacttct tattgaagtg aattcctgca tttgatagca atgtaagtgc 3077
 ctataaccat gttctatatt ctttattctc agtaactttt aaaaggaag ttatttatat 3137
 tttgtgtata atgtgcttta tttgcaaact acccactcct ttacaacat actttatata 3197
 tgtacatata ttcatactgt agaaaccagc tcatgtgtac ctcatatccc atccttaaga 3257
 gaagaaatgt tataaagtag aactaaatat aaattttcag aattaatgca ttcaaagtaa 3317
 tatatcaa atccaggacttt gttaacttca ggtaaaaact tcattagggt aatatcatct 3377
 caattttttc aaatgaaagg attctcta attagaaatt tatgtcagag ctgttataaa 3437
 tttatcaact gtcaaata tttctggacag ctaaactcatt tgagattttt gggtttttga 3497
 tttctattcc ctaacttgtg aagacaatga aaaatcaggc agaaatattt agtatctagt 3557
 cagtatctgt agctacactg tataactggt cttcaataaa atgggttcata ttttatagaa 3617
 aaaaaaaaaa aaaa 3631

<210> 21

<211> 19

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic primer

<400> 21

agatgctcac tgcgctgga

19

<210> 22

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic primer

<400> 22
tccaatgcag gcaatctgtt 20

<210> 23
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
primer

<400> 23
tggcactggg atgaaatca 19

<210> 24
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
primer

<400> 24
tggttacata aattggtccg a 21

<210> 25
<211> 465
<212> PRT
<213> Homo sapiens

<400> 25
Met Asn Val Thr Ser Leu Phe Ser Phe Thr Ser Pro Ala Val Lys Arg
1 5 10 15
Leu Leu Gly Trp Lys Gln Gly Asp Glu Glu Glu Lys Trp Ala Glu Lys
20 25 30
Ala Val Asp Ala Leu Val Lys Lys Leu Lys Lys Lys Lys Gly Ala Met
35 40 45
Glu Glu Leu Glu Lys Ala Leu Ser Cys Pro Gly Gln Pro Ser Asn Cys
50 55 60
Val Thr Ile Pro Arg Ser Leu Asp Gly Arg Leu Gln Val Ser His Arg
65 70 75 80
Lys Gly Leu Pro His Val Ile Tyr Cys Arg Val Trp Arg Trp Pro Asp
85 90 95
Leu Gln Ser His His Glu Leu Lys Pro Leu Glu Cys Cys Glu Phe Pro
100 105 110

Phe Gly Ser Lys Gln Lys Glu Val Cys Ile Asn Pro Tyr His Tyr Lys	115	120	125
Arg Val Glu Ser Pro Val Leu Pro Pro Val Leu Val Pro Arg His Ser	130	135	140
Glu Tyr Asn Pro Gln His Ser Leu Leu Ala Gln Phe Arg Asn Leu Gly	145	150	155 160
Gln Asn Glu Pro His Met Pro Leu Asn Ala Thr Phe Pro Asp Ser Phe	165	170	175
Gln Gln Pro Asn Ser His Pro Phe Pro His Ser Pro Asn Ser Ser Tyr	180	185	190
Pro Asn Ser Pro Gly Ser Ser Ser Ser Thr Tyr Pro His Ser Pro Thr	195	200	205
Ser Ser Asp Pro Gly Ser Pro Phe Gln Met Pro Ala Asp Thr Pro Pro	210	215	220
Pro Ala Tyr Leu Pro Pro Glu Asp Pro Met Thr Gln Asp Gly Ser Gln	225	230	235 240
Pro Met Asp Thr Asn Met Met Ala Pro Pro Leu Pro Ser Glu Ile Asn	245	250	255
Arg Gly Asp Val Gln Ala Val Ala Tyr Glu Glu Pro Lys His Trp Cys	260	265	270
Ser Ile Val Tyr Tyr Glu Leu Asn Asn Arg Val Gly Glu Ala Phe His	275	280	285
Ala Ser Ser Thr Ser Val Leu Val Asp Gly Phe Thr Asp Pro Ser Asn	290	295	300
Asn Lys Asn Arg Phe Cys Leu Gly Leu Leu Ser Asn Val Asn Arg Asn	305	310	315 320
Ser Thr Ile Glu Asn Thr Arg Arg His Ile Gly Lys Gly Val His Leu	325	330	335
Tyr Tyr Val Gly Gly Glu Val Tyr Ala Glu Cys Leu Ser Asp Ser Ser	340	345	350
Ile Phe Val Gln Ser Arg Asn Cys Asn Tyr His His Gly Phe His Pro	355	360	365
Thr Thr Val Cys Lys Ile Pro Ser Gly Cys Ser Leu Lys Ile Phe Asn	370	375	380
Asn Gln Glu Phe Ala Gln Leu Leu Ala Gln Ser Val Asn His Gly Phe	385	390	395 400
Glu Thr Val Tyr Glu Leu Thr Lys Met Cys Thr Ile Arg Met Ser Phe	405	410	415

Val Lys Gly Trp Gly Ala Glu Tyr His Arg Gln Asp Val Thr Ser Thr
 420 425 430

Pro Cys Trp Ile Glu Ile His Leu His Gly Pro Leu Gln Trp Leu Asp
 435 440 445

Lys Val Leu Thr Gln Met Gly Ser Pro His Asn Pro Ile Ser Ser Val
 450 455 460

Ser
 465

<210> 26

<211> 503

<212> PRT

<213> Homo sapiens

<400> 26

Met Thr Leu Gly Ser Pro Arg Lys Gly Leu Leu Met Leu Leu Met Ala
 1 5 10 15

Leu Val Thr Gln Gly Asp Pro Val Lys Pro Ser Arg Gly Pro Leu Val
 20 25 30

Thr Cys Thr Cys Glu Ser Pro His Cys Lys Gly Pro Thr Cys Arg Gly
 35 40 45

Ala Trp Cys Thr Val Val Leu Val Arg Glu Glu Gly Arg His Pro Gln
 50 55 60

Glu His Arg Gly Cys Gly Asn Leu His Arg Glu Leu Cys Arg Gly Arg
 65 70 75 80

Pro Thr Glu Phe Val Asn His Tyr Cys Cys Asp Ser His Leu Cys Asn
 85 90 95

His Asn Val Ser Leu Val Leu Glu Ala Thr Gln Pro Pro Ser Glu Gln
 100 105 110

Pro Gly Thr Asp Gly Gln Leu Ala Leu Ile Leu Gly Pro Val Leu Ala
 115 120 125

Leu Leu Ala Leu Val Ala Leu Gly Val Leu Gly Leu Trp His Val Arg
 130 135 140

Arg Arg Gln Glu Lys Gln Arg Gly Leu His Ser Glu Leu Gly Glu Ser
 145 150 155 160

Ser Leu Ile Leu Lys Ala Ser Glu Gln Gly Asp Thr Met Leu Gly Asp
 165 170 175

Leu Leu Asp Ser Asp Cys Thr Thr Gly Ser Gly Ser Gly Leu Pro Phe
 180 185 190

Leu Val Gln Arg Thr Val Ala Arg Gln Val Ala Leu Val Glu Cys Val
 195 200 205

Gly Lys Gly Arg Tyr Gly Glu Val Trp Arg Gly Leu Trp His Gly Glu
 210 215 220
 Ser Val Ala Val Lys Ile Phe Ser Ser Arg Asp Glu Gln Ser Trp Phe
 225 230 235 240
 Arg Glu Thr Glu Ile Tyr Asn Thr Val Leu Leu Arg His Asp Asn Ile
 245 250 255
 Leu Gly Phe Ile Ala Ser Asp Met Thr Ser Arg Asn Ser Ser Thr Gln
 260 265 270
 Leu Trp Leu Ile Thr His Tyr His Glu His Gly Ser Leu Tyr Asp Phe
 275 280 285
 Leu Gln Arg Gln Thr Leu Glu Pro His Leu Ala Leu Arg Leu Ala Val
 290 295 300
 Ser Ala Ala Cys Gly Leu Ala His Leu His Val Glu Ile Phe Gly Thr
 305 310 315 320
 Gln Gly Lys Pro Ala Ile Ala His Arg Asp Phe Lys Ser Arg Asn Val
 325 330 335
 Leu Val Lys Ser Asn Leu Gln Cys Cys Ile Ala Asp Leu Gly Leu Ala
 340 345 350
 Val Met His Ser Gln Gly Ser Asp Tyr Leu Asp Ile Gly Asn Asn Pro
 355 360 365
 Arg Val Gly Thr Lys Arg Tyr Met Ala Pro Glu Val Leu Asp Glu Gln
 370 375 380
 Ile Arg Thr Asp Cys Phe Glu Ser Tyr Lys Trp Thr Asp Ile Trp Ala
 385 390 395 400
 Phe Gly Leu Val Leu Trp Glu Ile Ala Arg Arg Thr Ile Val Asn Gly
 405 410 415
 Ile Val Glu Asp Tyr Arg Pro Pro Phe Tyr Asp Val Val Pro Asn Asp
 420 425 430
 Pro Ser Phe Glu Asp Met Lys Lys Val Val Cys Val Asp Gln Gln Thr
 435 440 445
 Pro Thr Ile Pro Asn Arg Leu Ala Ala Asp Pro Val Leu Ser Gly Leu
 450 455 460
 Ala Gln Met Met Arg Glu Cys Trp Tyr Pro Asn Pro Ser Ala Arg Leu
 465 470 475 480
 Thr Ala Leu Arg Ile Lys Lys Thr Leu Gln Lys Ile Ser Asn Ser Pro
 485 490 495
 Glu Lys Pro Lys Val Ile Gln
 500

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<210> 27
<211> 396
<212> PRT
<213> Homo sapiens
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<400> 27																
Met	Val	Ala	Gly	Thr	Arg	Cys	Leu	Leu	Ala	Leu	Leu	Leu	Pro	Gln	Val	
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Leu	Leu	Gly	Gly	Ala	Ala	Gly	Leu	Val	Pro	Glu	Leu	Gly	Arg	Arg	Lys	
			20					25					30			
Phe	Ala	Ala	Ala	Ser	Ser	Gly	Arg	Pro	Ser	Ser	Gln	Pro	Ser	Asp	Glu	
		35					40					45				
Val	Leu	Ser	Glu	Phe	Glu	Leu	Arg	Leu	Leu	Ser	Met	Phe	Gly	Leu	Lys	
	50					55					60					
Gln	Arg	Pro	Thr	Pro	Ser	Arg	Asp	Ala	Val	Val	Pro	Pro	Tyr	Met	Leu	
65					70					75					80	
Asp	Leu	Tyr	Arg	Arg	His	Ser	Gly	Gln	Pro	Gly	Ser	Pro	Ala	Pro	Asp	
				85					90					95		
His	Arg	Leu	Glu	Arg	Ala	Ala	Ser	Arg	Ala	Asn	Thr	Val	Arg	Ser	Phe	
			100					105					110			
His	His	Glu	Glu	Ser	Leu	Glu	Glu	Leu	Pro	Glu	Thr	Ser	Gly	Lys	Thr	
	115						120					125				
Thr	Arg	Arg	Phe	Phe	Phe	Asn	Leu	Ser	Ser	Ile	Pro	Thr	Glu	Glu	Phe	
	130					135					140					
Ile	Thr	Ser	Ala	Glu	Leu	Gln	Val	Phe	Arg	Glu	Gln	Met	Gln	Asp	Ala	
145					150					155					160	
Leu	Gly	Asn	Asn	Ser	Ser	Phe	His	His	Arg	Ile	Asn	Ile	Tyr	Glu	Ile	
				165					170					175		
Ile	Lys	Pro	Ala	Thr	Ala	Asn	Ser	Lys	Phe	Pro	Val	Thr	Arg	Leu	Leu	
			180					185					190			
Asp	Thr	Arg	Leu	Val	Asn	Gln	Asn	Ala	Ser	Arg	Trp	Glu	Ser	Phe	Asp	
	195					200						205				
Val	Thr	Pro	Ala	Val	Met	Arg	Trp	Thr	Ala	Gln	Gly	His	Ala	Asn	His	
	210					215					220					
Gly	Phe	Val	Val	Glu	Val	Ala	His	Leu	Glu	Glu	Lys	Gln	Gly	Val	Ser	
225				230					235						240	
Lys	Arg	His	Val	Arg	Ile	Ser	Arg	Ser	Leu	His	Gln	Asp	Glu	His	Ser	
				245					250					255		
Trp	Ser	Gln	Ile	Arg	Pro	Leu	Leu	Val	Thr	Phe	Gly	His	Asp	Gly	Lys	
			260					265					270			

Gly His Pro Leu His Lys Arg Glu Lys Arg Gln Ala Lys His Lys Gln
 275 280 285
 Arg Lys Arg Leu Lys Ser Ser Cys Lys Arg His Pro Leu Tyr Val Asp
 290 295 300
 Phe Ser Asp Val Gly Trp Asn Asp Trp Ile Val Ala Pro Pro Gly Tyr
 305 310 315 320
 His Ala Phe Tyr Cys His Gly Glu Cys Pro Phe Pro Leu Ala Asp His
 325 330 335
 Leu Asn Ser Thr Asn His Ala Ile Val Gln Thr Leu Val Asn Ser Val
 340 345 350
 Asn Ser Lys Ile Pro Lys Ala Cys Cys Val Pro Thr Glu Leu Ser Ala
 355 360 365
 Ile Ser Met Leu Tyr Leu Asp Glu Asn Glu Lys Val Val Leu Lys Asn
 370 375 380
 Tyr Gln Asp Met Val Val Glu Gly Cys Gly Cys Arg
 385 390 395

<210> 28
 <211> 408
 <212> PRT
 <213> Homo sapiens

<400> 28
 Met Ile Pro Gly Asn Arg Met Leu Met Val Val Leu Leu Cys Gln Val
 1 5 10 15
 Leu Leu Gly Gly Ala Ser His Ala Ser Leu Ile Pro Glu Thr Gly Lys
 20 25 30
 Lys Lys Val Ala Glu Ile Gln Gly His Ala Gly Gly Arg Arg Ser Gly
 35 40 45
 Gln Ser His Glu Leu Leu Arg Asp Phe Glu Ala Thr Leu Leu Gln Met
 50 55 60
 Phe Gly Leu Arg Arg Arg Pro Gln Pro Ser Lys Ser Ala Val Ile Pro
 65 70 75 80
 Asp Tyr Met Arg Asp Leu Tyr Arg Leu Gln Ser Gly Glu Glu Glu Glu
 85 90 95
 Glu Gln Ile His Ser Thr Gly Leu Glu Tyr Pro Glu Arg Pro Ala Ser
 100 105 110
 Arg Ala Asn Thr Val Arg Ser Phe His His Glu Glu His Leu Glu Asn
 115 120 125
 Ile Pro Gly Thr Ser Glu Asn Ser Ala Phe Arg Phe Leu Phe Asn Leu
 130 135 140

Ser Ser Ile Pro Glu Asn Glu Ala Ile Ser Ser Ala Glu Leu Arg Leu
 145 150 155 160
 Phe Arg Glu Gln Val Asp Gln Gly Pro Asp Trp Glu Arg Gly Phe His
 165 170 175
 Arg Ile Asn Ile Tyr Glu Val Met Lys Pro Pro Ala Glu Val Val Pro
 180 185 190
 Gly His Leu Ile Thr Arg Leu Leu Asp Thr Arg Leu Val His His Asn
 195 200 205
 Val Thr Arg Trp Glu Thr Phe Asp Val Ser Pro Ala Val Leu Arg Trp
 210 215 220
 Thr Arg Glu Lys Gln Pro Asn Tyr Gly Leu Ala Ile Glu Val Thr His
 225 230 235 240
 Leu His Gln Thr Arg Thr His Gln Gly Gln His Val Arg Ile Ser Arg
 245 250 255
 Ser Leu Pro Gln Gly Ser Gly Asn Trp Ala Gln Leu Arg Pro Leu Leu
 260 265 270
 Val Thr Phe Gly His Asp Gly Arg Gly His Ala Leu Thr Arg Arg Arg
 275 280 285
 Arg Ala Lys Arg Ser Pro Lys His His Ser Gln Arg Ala Arg Lys Lys
 290 295 300
 Asn Lys Asn Cys Arg Arg His Ser Leu Tyr Val Asp Phe Ser Asp Val
 305 310 315 320
 Gly Trp Asn Asp Trp Ile Val Ala Pro Pro Gly Tyr Gln Ala Phe Tyr
 325 330 335
 Cys His Gly Asp Cys Pro Phe Pro Leu Ala Asp His Leu Asn Ser Thr
 340 345 350
 Asn His Ala Ile Val Gln Thr Leu Val Asn Ser Val Asn Ser Ser Ile
 355 360 365
 Pro Lys Ala Cys Cys Val Pro Thr Glu Leu Ser Ala Ile Ser Met Leu
 370 375 380
 Tyr Leu Asp Glu Tyr Asp Lys Val Val Leu Lys Asn Tyr Gln Glu Met
 385 390 395 400
 Val Val Glu Gly Cys Gly Cys Arg
 405

<210> 29

<211> 770

<212> PRT

<213> Homo sapiens

<400> 29

Met	Ala	Gln	Trp	Asn	Gln	Leu	Gln	Gln	Leu	Asp	Thr	Arg	Tyr	Leu	Glu	1	5	10	15
Gln	Leu	His	Gln	Leu	Tyr	Ser	Asp	Ser	Phe	Pro	Met	Glu	Leu	Arg	Gln	20	25	30	
Phe	Leu	Ala	Pro	Trp	Ile	Glu	Ser	Gln	Asp	Trp	Ala	Tyr	Ala	Ala	Ser	35	40	45	
Lys	Glu	Ser	His	Ala	Thr	Leu	Val	Phe	His	Asn	Leu	Leu	Gly	Glu	Ile	50	55	60	
Asp	Gln	Gln	Tyr	Ser	Arg	Phe	Leu	Gln	Glu	Ser	Asn	Val	Leu	Tyr	Gln	65	70	75	80
His	Asn	Leu	Arg	Arg	Ile	Lys	Gln	Phe	Leu	Gln	Ser	Arg	Tyr	Leu	Glu	85	90	95	
Lys	Pro	Met	Glu	Ile	Ala	Arg	Ile	Val	Ala	Arg	Cys	Leu	Trp	Glu	Glu	100	105	110	
Ser	Arg	Leu	Leu	Gln	Thr	Ala	Ala	Thr	Ala	Ala	Gln	Gln	Gly	Gly	Gln	115	120	125	
Ala	Asn	His	Pro	Thr	Ala	Ala	Val	Val	Thr	Glu	Lys	Gln	Gln	Met	Leu	130	135	140	
Glu	Gln	His	Leu	Gln	Asp	Val	Arg	Lys	Arg	Val	Gln	Asp	Leu	Glu	Gln	145	150	155	160
Lys	Met	Lys	Val	Val	Glu	Asn	Leu	Gln	Asp	Asp	Phe	Asp	Phe	Asn	Tyr	165	170	175	
Lys	Thr	Leu	Lys	Ser	Gln	Gly	Asp	Met	Gln	Asp	Leu	Asn	Gly	Asn	Asn	180	185	190	
Gln	Ser	Val	Thr	Arg	Gln	Lys	Met	Gln	Gln	Leu	Glu	Gln	Met	Leu	Thr	195	200	205	
Ala	Leu	Asp	Gln	Met	Arg	Arg	Ser	Ile	Val	Ser	Glu	Leu	Ala	Gly	Leu	210	215	220	
Leu	Ser	Ala	Met	Glu	Tyr	Val	Gln	Lys	Thr	Leu	Thr	Asp	Glu	Glu	Leu	225	230	235	240
Ala	Asp	Trp	Lys	Arg	Arg	Gln	Gln	Ile	Ala	Cys	Ile	Gly	Gly	Pro	Pro	245	250	255	
Asn	Ile	Cys	Leu	Asp	Arg	Leu	Glu	Asn	Trp	Ile	Thr	Ser	Leu	Ala	Glu	260	265	270	
Ser	Gln	Leu	Gln	Thr	Arg	Gln	Gln	Ile	Lys	Lys	Leu	Glu	Glu	Leu	Gln	275	280	285	
Gln	Lys	Val	Ser	Tyr	Lys	Gly	Asp	Pro	Ile	Val	Gln	His	Arg	Pro	Met	290	295	300	

Leu Glu Glu Arg Ile Val Glu Leu Phe Arg Asn Leu Met Lys Ser Ala
 305 310 315 320
 Phe Val Val Glu Arg Gln Pro Cys Met Pro Met His Pro Asp Arg Pro
 325 330 335
 Leu Val Ile Lys Thr Gly Val Gln Phe Thr Thr Lys Val Arg Leu Leu
 340 345 350
 Val Lys Phe Pro Glu Leu Asn Tyr Gln Leu Lys Ile Lys Val Cys Ile
 355 360 365
 Asp Lys Asp Ser Gly Asp Val Ala Ala Leu Arg Gly Ser Arg Lys Phe
 370 375 380
 Asn Ile Leu Gly Thr Asn Thr Lys Val Met Asn Met Glu Glu Ser Asn
 385 390 395 400
 Asn Gly Ser Leu Ser Ala Glu Phe Lys His Leu Thr Leu Arg Glu Gln
 405 410 415
 Arg Cys Gly Asn Gly Gly Arg Ala Asn Cys Asp Ala Ser Leu Ile Val
 420 425 430
 Thr Glu Glu Leu His Leu Ile Thr Phe Glu Thr Glu Val Tyr His Gln
 435 440 445
 Gly Leu Lys Ile Asp Leu Glu Thr His Ser Leu Pro Val Val Val Ile
 450 455 460
 Ser Asn Ile Cys Gln Met Pro Asn Ala Trp Ala Ser Ile Leu Trp Tyr
 465 470 475 480
 Asn Met Leu Thr Asn Asn Pro Lys Asn Val Asn Phe Phe Thr Lys Pro
 485 490 495
 Pro Ile Gly Thr Trp Asp Gln Val Ala Glu Val Leu Ser Trp Gln Phe
 500 505 510
 Ser Ser Thr Thr Lys Arg Gly Leu Ser Ile Glu Gln Leu Thr Thr Leu
 515 520 525
 Ala Glu Lys Leu Leu Gly Pro Gly Val Asn Tyr Ser Gly Cys Gln Ile
 530 535 540
 Thr Trp Ala Lys Phe Cys Lys Glu Asn Met Ala Gly Lys Gly Phe Ser
 545 550 555 560
 Phe Trp Val Trp Leu Asp Asn Ile Ile Asp Leu Val Lys Lys Tyr Ile
 565 570 575
 Leu Ala Leu Trp Asn Glu Gly Tyr Ile Met Gly Phe Ile Ser Lys Glu
 580 585 590
 Arg Glu Arg Ala Ile Leu Ser Thr Lys Pro Pro Gly Thr Phe Leu Leu
 595 600 605

Arg Phe Ser Glu Ser Ser Lys Glu Gly Gly Val Thr Phe Thr Trp Val
 610 615 620
 Glu Lys Asp Ile Ser Gly Lys Thr Gln Ile Gln Ser Val Glu Pro Tyr
 625 630 635 640
 Thr Lys Gln Gln Leu Asn Asn Met Ser Phe Ala Glu Ile Ile Met Gly
 645 650 655
 Tyr Lys Ile Met Asp Ala Thr Asn Ile Leu Val Ser Pro Leu Val Tyr
 660 665 670
 Leu Tyr Pro Asp Ile Pro Lys Glu Glu Ala Phe Gly Lys Tyr Cys Arg
 675 680 685
 Pro Glu Ser Gln Glu His Pro Glu Ala Asp Pro Gly Ser Ala Ala Pro
 690 695 700
 Tyr Leu Lys Thr Lys Phe Ile Cys Val Thr Pro Thr Thr Cys Ser Asn
 705 710 715 720
 Thr Ile Asp Leu Pro Met Ser Pro Arg Thr Leu Asp Ser Leu Met Gln
 725 730 735
 Phe Gly Asn Asn Gly Glu Gly Ala Glu Pro Ser Ala Gly Gly Gln Phe
 740 745 750
 Glu Ser Leu Thr Phe Asp Met Glu Leu Thr Ser Glu Cys Ala Thr Ser
 755 760 765
 Pro Met
 770

<210> 30
 <211> 532
 <212> PRT
 <213> Homo sapiens

<400> 30
 Met Pro Gln Leu Tyr Ile Tyr Ile Arg Leu Leu Gly Ala Tyr Leu Phe
 1 5 10 15
 Ile Ile Ser Arg Val Gln Gly Gln Asn Leu Asp Ser Met Leu His Gly
 20 25 30
 Thr Gly Met Lys Ser Asp Ser Asp Gln Lys Lys Ser Glu Asn Gly Val
 35 40 45
 Thr Leu Ala Pro Glu Asp Thr Leu Pro Phe Leu Lys Cys Tyr Cys Ser
 50 55 60
 Gly His Cys Pro Asp Asp Ala Ile Asn Asn Thr Cys Ile Thr Asn Gly
 65 70 75 80
 His Cys Phe Ala Ile Ile Glu Glu Asp Asp Gln Gly Glu Thr Thr Leu
 85 90 95

Ala	Ser	Gly	Cys	Met	Lys	Tyr	Glu	Gly	Ser	Asp	Phe	Gln	Cys	Lys	Asp		
			100					105					110				
Ser	Pro	Lys	Ala	Gln	Leu	Arg	Arg	Thr	Ile	Glu	Cys	Cys	Arg	Thr	Asn		
		115					120					125					
Leu	Cys	Asn	Gln	Tyr	Leu	Gln	Pro	Thr	Leu	Pro	Pro	Val	Val	Ile	Gly		
	130					135					140						
Pro	Phe	Phe	Asp	Gly	Ser	Ile	Arg	Trp	Leu	Val	Leu	Leu	Ile	Ser	Met		
145					150					155					160		
Ala	Val	Cys	Ile	Ile	Ala	Met	Ile	Ile	Phe	Ser	Ser	Cys	Phe	Cys	Tyr		
			165						170					175			
Lys	His	Tyr	Cys	Lys	Ser	Ile	Ser	Ser	Arg	Arg	Arg	Tyr	Asn	Arg	Asp		
		180						185					190				
Leu	Glu	Gln	Asp	Glu	Ala	Phe	Ile	Pro	Val	Gly	Glu	Ser	Leu	Lys	Asp		
	195						200					205					
Leu	Ile	Asp	Gln	Ser	Gln	Ser	Ser	Gly	Ser	Gly	Ser	Gly	Leu	Pro	Leu		
	210					215					220						
Leu	Val	Gln	Arg	Thr	Ile	Ala	Lys	Gln	Ile	Gln	Met	Val	Arg	Gln	Val		
225					230					235					240		
Gly	Lys	Gly	Arg	Tyr	Gly	Glu	Val	Trp	Met	Gly	Lys	Trp	Arg	Gly	Glu		
			245						250					255			
Lys	Val	Ala	Val	Lys	Val	Phe	Phe	Thr	Thr	Glu	Glu	Ala	Ser	Trp	Phe		
			260					265					270				
Arg	Glu	Thr	Glu	Ile	Tyr	Gln	Thr	Val	Leu	Met	Arg	His	Glu	Asn	Ile		
	275						280					285					
Leu	Gly	Phe	Ile	Ala	Ala	Asp	Ile	Lys	Gly	Thr	Gly	Ser	Trp	Thr	Gln		
	290					295					300						
Leu	Tyr	Leu	Ile	Thr	Asp	Tyr	His	Glu	Asn	Gly	Ser	Leu	Tyr	Asp	Phe		
305					310					315					320		
Leu	Lys	Cys	Ala	Thr	Leu	Asp	Thr	Arg	Ala	Leu	Leu	Lys	Leu	Ala	Tyr		
			325						330					335			
Ser	Ala	Ala	Cys	Gly	Leu	Cys	His	Leu	His	Thr	Glu	Ile	Tyr	Gly	Thr		
			340					345					350				
Gln	Gly	Lys	Pro	Ala	Ile	Ala	His	Arg	Asp	Leu	Lys	Ser	Lys	Asn	Ile		
	355						360					365					
Leu	Ile	Lys	Lys	Asn	Gly	Ser	Cys	Cys	Ile	Ala	Asp	Leu	Gly	Leu	Ala		
	370					375					380						
Val	Lys	Phe	Asn	Ser	Asp	Thr	Asn	Glu	Val	Asp	Val	Pro	Leu	Asn	Thr		
385					390					395					400		

Arg	Val	Gly	Thr	Lys	Arg	Tyr	Met	Ala	Pro	Glu	Val	Leu	Asp	Glu	Ser	405	410	415	
Leu	Asn	Lys	Asn	His	Phe	Gln	Pro	Tyr	Ile	Met	Ala	Asp	Ile	Tyr	Ser	420	425	430	
Phe	Gly	Leu	Ile	Ile	Trp	Glu	Met	Ala	Arg	Arg	Cys	Ile	Thr	Gly	Gly	435	440	445	
Ile	Val	Glu	Glu	Tyr	Gln	Leu	Pro	Tyr	Tyr	Asn	Met	Val	Pro	Ser	Asp	450	455	460	
Pro	Ser	Tyr	Glu	Asp	Met	Arg	Glu	Val	Val	Cys	Val	Lys	Arg	Leu	Arg	465	470	475	480
Pro	Ile	Val	Ser	Asn	Arg	Trp	Asn	Ser	Asp	Glu	Cys	Leu	Arg	Ala	Val	485	490	495	
Leu	Lys	Leu	Met	Ser	Glu	Cys	Trp	Ala	His	Asn	Pro	Ala	Ser	Arg	Leu	500	505	510	
Thr	Ala	Leu	Arg	Ile	Lys	Lys	Thr	Leu	Ala	Lys	Met	Val	Glu	Ser	Gln	515	520	525	
Asp	Val	Lys	Ile													530			